

AMENDMENTS TO THE SPECIFICATION

IN THE SPECIFICATION:

Before line 1 of the specification, please insert the following new paragraph:

This application is a Divisional of co-pending Application No. 09/763,985, filed on February 28, 2001, the entire contents of which are hereby incorporated by reference and for which priority is claimed under 35 U.S.C. § 120; and this application claims priority of Application No. 242660/1998 filed in Japan on August 28, 1998, under 35 U.S.C. § 119, and International Application No. PCT/JP99/04622 filed on August 27, 1999 under 35 U.S.C. § 120 and the Patent Cooperation Treaty.

The paragraph beginning on page 6, line 16 has been amended as follows:

Thus, the present invention relates to:

(1) A DNA encoding a protein consisting of an amino acid sequence shown in SEQ ID NO: 21, or a protein variant consisting of an amino acid sequence containing substitution, deletion, and/or addition of one or more amino acid residues of SEQ ID NO: 21, provided that the protein and the protein variant give rise to tumor antigen peptides that are capable of binding to an HLA antigen and being recognized by cytotoxic T lymphocytes;

The paragraph beginning on page 6, line 24 has been amended as follows:

(2) A DNA consisting of a base sequence shown in SEQ ID NO: 12, or a DNA variant that hybridizes to the DNA under a stringent condition, provided that a protein produced and expressed by the DNA or the DNA variant gives rise to tumor antigen peptides that are capable of binding to an HLA antigen and being recognized by cytotoxic T lymphocytes;

The paragraph beginning on page 11, line 5 has been amended as follows:

The DNAs of the present invention encode novel tumor antigen proteins, and specific examples of the DNAs include a DNA encoding SART-3 protein consisting of an amino acid sequence shown in SEQ ID NO: 21, or a protein variant consisting of an amino acid sequence containing substitution, deletion, and/or addition of one or more amino acid residues of the amino acid sequence of SART-3, provided that the protein and the protein variant give rise to tumor antigen peptides that are capable of binding to an HLA antigen and being recognized by cytotoxic T lymphocytes; or a DNA of SART-3 consisting of a base sequence shown in SEQ ID NO: 12, or a DNA variant that hybridizes to the DNA of SART-3 under a stringent condition, provided that a protein produced and

expressed by the DNA and the DNA variant gives rise to tumor antigen peptides that are capable of binding to an HLA antigen and being recognized by cytotoxic T lymphocytes. The DNA of the present invention is further described hereinafter following the order established above.

The paragraph beginning on page 11, line 21 has been amended as follows:

1) DNA encoding SART-3

"DNA encoding a protein consisting of an amino acid sequence shown in SEQ ID NO: 21" and "a DNA consisting of a base sequence shown in SEQ ID NO: 12" among the DNAs described above refers to a DNA encoding tumor antigen protein SART-3 of the present invention. The DNA may be cloned in accordance with the process described in Examples hereinafter. Further, the cloning of the DNA may be also conducted by, for example, screening a cDNA library derived from cell lines such as esophageal cancer cell line KE-4 (FERM BP-5955) using an appropriate portion of the base sequence disclosed in GenBank Accession No. D63879 or shown in SEQ ID NO: 12 in the present specification as a probe for hybridization or a PCR primer. It would be ready for those skilled in the art to achieve such cloning in accordance with Molecular Cloning 2nd Edt. Cold Spring Harbor Laboratory Press (1989), for example.

The paragraph beginning on page 12, line 25 has been amended as follows:

3) DNA that hybridizes to the DNA of SART-3 under a stringent condition

"DNA variant that hybridizes to the DNA of SART-3 under a stringent condition" among the DNAs described above refers to a DNA that hybridizes to human SART-3 cDNA consisting of the base sequence shown in SEQ ID NO: 12 under a stringent condition, including SART-3 DNAs from all of vertebrate such as rat and mouse, and DNAs encoding a partial protein of SART-3.

The paragraph beginning on page 13, line 14 has been amended as follows:

The DNA variants are cloned by diverse processes such as hybridization to the DNA shown in SEQ ID NO: 12. Particular procedures for the processes such as production of cDNA library, hybridization, selection of positive colony, and determination of base sequence are well-known, and may be conducted consulting Molecular Cloning as shown above. Probes useful for the hybridization includes a DNA comprising a base sequence described in SEQ ID NO: 12.

The paragraph beginning on page 17, line 12 has been amended as follows:

In the invention, the term "protein" refers to a protein encoded by the various DNAs of the present invention as described above, which has an ability as tumor antigen protein to give rise to tumor antigen peptides via intracellular degradation that are capable of binding to an HLA antigen and being recognized by CTLs. Specific examples of the proteins include SART-3 comprising an amino acid sequence shown in SEQ ID NO: 21. The proteins of the present invention may be produced in large scale using the DNA of the present invention as described above.

Please amend the paragraph on page 21, lines 23-25 as follows:

In addition, any peptide sequence expected to be capable of binding to HLA antigens may be searched on internet using a software of NIH BIMAS (~~http://bimas.dert.nih.gov/molbio/hla_bind/~~).

The paragraph beginning on page 22, line 5 has been amended as follows:

It is easy to select peptide portions involved in such motifs from the amino acid sequence of the protein of the present invention. Such peptide portions involved in the above motif structures can be easily selected by inspecting

the amino acid sequence of tumor antigen protein SART-3 (SEQ ID NO: 24). Further, it is easy to select any sequence expected to be capable of binding to HLA antigens by search on internet as shown above. Tumor antigen peptides of the present invention can be identified by synthesizing candidate peptides thus selected according to the method described above and conducting an assay for determining whether or not a complex between the candidate peptide and an HLA antigen is recognized by CTL, in other words, whether or not a candidate peptide has an activity as a tumor antigen peptide.

Please amend the paragraph on page 24, line 18 to page 25, line 6, as follows:

As described above, it is known that the sequences of tumor antigen peptides that are bound to and presented on HLA-A24 obey a certain rule (motif), and in particular, the motif is that, in a sequence of a peptide consisting of 8 to 11 amino acids, the amino acid at position 2 is tyrosine, phenylalanine, methionine, or tryptophan, and the amino acid at the C-terminus is phenylalanine, leucine, isoleucine, tryptophan, or methionine (*J. Immunol.*, 152:3913, 1994; *Immunogenetics*, 41:p178, 1995; *J. Immunol.*, 155:p4307, 1994). Likewise, a similar rule (motif) can be found in the sequences of tumor antigen peptides that are bound to and presented on HLA-A2, and in particular, the motifs shown in the

above Table 1 are known (*Immunogenetics*, 41, p178, 1995; *J. Immunol.*, 155:p4749, 1995). As shown above, sequences expected to be capable of binding to HLA antigens may be further searched on internet using NIH BIMAS software (~~http://bimas.dert.nih.gov/molbio/hla_bind/~~).

The paragraph beginning on page 25, line 7 has been amended as follows:

Accordingly, HLA-A24- and HLA-A2-restricted tumor antigen peptides among the tumor antigen peptides of the present invention are exemplified by those tumor antigen peptides that are partial peptides involved in such motif structures or structures expected to be capable of binding to the HLAs in the amino acid sequence of SART-3 shown in SEQ ID NO: 21 and that are capable of binding to respective HLA antigens and being recognized by CTLs.

Please amend the paragraph on page 29, lines 1-10 as follows:

As described above, the sequence rules (motifs) for peptides that are bound to and presented on HLA types such as HLA-A1, -A0201, -A0204, -A0205, -A0206, -A0207, -A11, -A24, -A31, -A6801, -B7, -B8, -B2705, -B37, -Cw0401, and -Cw0602 have been elucidated. As shown above, peptide sequences expected to be capable of binding to HLA antigens may be further searched on internet

~~(http://bimas.dert.nih.gov/molbio/hla_bind/)~~. Consequently, tumor antigen peptide derivatives containing the alteration of the amino acids in a tumor antigen peptide of the present invention can be prepared on the basis of such motifs.

Please amend the paragraph on page 29, lines 11 to page 30, line 13, as follows:

For example, regarding the motif for antigen peptides that are bound to and presented on HLA-A24, it is known as described above that in the sequence of a peptide consisting of 8 to 11 amino acids, the amino acid at position 2 is tyrosine, phenylalanine, methionine, or tryptophan, and the amino acid at the C-terminus is phenylalanine, leucine, isoleucine, tryptophan, or methionine (*J. Immunol.*, 152:3913, 1994; *Immunogenetics*, 41:178, 1995; *J. Immunol.*, 155:4307, 1994). Likewise, the motifs shown in the above Table 1 are known for HLA-A2. In addition, peptide sequences expected to be capable of binding to HLA antigens is laid open on internet ~~(http://bimas.dert.nih.gov/molbio/hla_bind/)~~, and amino acid residues having properties similar to those of amino acids according to the motifs may also be possible. Accordingly, examples of tumor antigen peptide derivatives of the present invention include those peptide derivatives that comprise all or part of an amino acid sequence of the tumor antigen peptide of the present invention in which one or more amino acid residues at any

positions that may be allowed for substitution according to the motifs (for HLA-A24 and HLA-A2, position 2 and the C-terminus) are substituted by other amino acids (preferably, which is the amino acid expected to be capable of binding to the antigens according to the above internet), and which derivatives have activity of binding to HLA antigens and being recognized by CTLs. Preferred examples are those tumor antigen peptide derivatives that comprise all or part of an amino acid sequence in which amino acid residues to be substituted are selected from those at said positions according to the above motifs, and which derivatives have the above activity. A preferred length of "all or part" of an amino acid sequence is about 8 to 14 amino acids, although it may be a length of 14 or more amino acids for HLA-DR, -DP, and -DQ.

The paragraph beginning on page 48, line 19 has been amended as follows:

Determination of Base Sequence of Tumor Antigen Protein
Gene

The base sequence of the DNA of tumor antigen protein SART-3 as obtained in Example 3 was determined using DyeDeoxy Terminator Cycle Sequencing kit (Perkin-Elmer). The base sequence thus determined is shown in SEQ ID NO: 12. The full-length of the cDNA was 3798 base pairs. Amino acid sequence

(963 amino acids) encoded by the base sequence of SEQ ID NO: 12 is shown in SEQ ID NO: 21. Comparison of the base sequence shown in SEQ ID NO: 12 to known sequences using GenBank data base revealed that the base sequence of tumor antigen protein SART-3 has a novel base sequence that is different from gene KIAA0156 registered at GenBank under Accession No. D63879 in terms of a single base (at position 108 of KIAA0156), which function has not been demonstrated.

The paragraph beginning on page 49, line 10 has been amended as follows:

Selection of Candidate Peptides

There are certain rules (motifs) in the sequences of antigen peptides that should be bound and presented by HLA antigens. Regarding the motif for HLA-A24, it is known that in the sequence of peptides consisting of 8 to 11 amino acids, the amino acid at position 2 is tyrosine, phenylalanine, methionine, or tryptophan, and the amino acid at the C-terminus is phenylalanine, tryptophan, leucine, isoleucine, or methionine (*Immunogenetics*, 41:178, 1995; *J. Immunol.*, 152:3913, 1994; *J. Immunol.*, 155:4307, 1994). According to the motifs, peptide portions consisting of 8 to 11 peptides having the above motifs were selected from the amino acid sequence of tumor antigen protein SART-3 shown in SEQ ID NO:

21. Those examples of the selected peptides are shown in SEQ ID NOs: 3-24. These peptides were synthesized at Biologica Co. by the Fmoc method.

The paragraph on page 51, line 21 has been amended as follows:

To this peptide resin, 2 ml of Reagent K (the solution of 5% phenol, 5% thioanisole, 5% H₂O, and 2.5% ethanedithiol in TFA) was added and the mixture was allowed to react for 2.5 hours at room temperature. While cooling with ice, 10 ml of diethyl ether was added to the reaction, the mixture was stirred for 10 minutes, filtered, and washed with 10 ml of diethyl ether. To the filter cake, 10 ml of aqueous acetic acid was added, and the mixture was stirred for 30 minutes. The resin was then filtered, and washed with 4 ml of aqueous acetic acid. After lyophilizing the filtrate and the wash, the crude peptide obtained was dissolved in aqueous acetic acid, and injected into a reverse phase packing material, YMC-PACK ODS-A column (30 ϕ x 250 mm) that had been pre-equilibrated with 0.1% aqueous TFA. The column was washed with 0.1% aqueous TFA, and elution at a flow rate of 7 ml/min was then conducted, while increasing the concentration of acetonitrile up to 25% over 180 minutes. The eluate was monitored by A 220 nm. The fractions containing the desired

product were combined together and lyophilized to obtain 31.0 mg of Val-Tyr-Asp-Tyr-Asn-Cys-His-Val-Asp-Leu(SEQ ID NO:3).

The paragraph beginning on page 52, line 13 has been amended as follows:

The peptide obtained, Val-Tyr-Asp-Tyr-Asn-Cys-His-Val-Asp-Leu(SEQ ID NO:3), had a retention time of 19.3 minutes in an analysis using a reverse phase packing material, YMC-PACK ODS-AM column (4.6 ϕ x 250 mm) eluted with a linear gradient of acetonitrile concentration from 16 to 46% containing 0.1% TFA, and the results of amino acid analysis (Cys being not detected) and mass spectrometry of the product were consistent with the theoretical values.

The paragraph beginning on page 53, line 21 has been amended as follows:

(2) Synthesis of SART-3 "172-181" Leu-Phe-Glu-Lys-Ala-Val-Lys-Asp-Tyr-Ile (SEQ ID NO: 4)

According to a similar manner to that described in above (1), using 100 mg of Fmoc-Ile-Alko Resin (0.41mmol/g, 100-200mesh), Fmoc-Tyr(tBu)-OH, Fmoc-Asp(OtBu)-OH, Fmoc-Lys(Boc)-OH, Fmoc-Val-OH, Fmoc-Ala-OH, Fmoc-Lys(Boc)-OH, Fmoc-Glu(OtBu)-OH, Fmoc-Phe-OH, and Fmoc-Leu-OH were coupled in order, and the product was then deprotected. The crude

peptide obtained was dissolved in aqueous acetic acid and injected into a reverse phase packing material YMC-PACK ODS-A column (30 ϕ x 250 mm) that has been pre-equilibrated with 0.1% aqueous TFA. The column was washed with 0.1% aqueous TFA, and the elution at a flow rate of 7 ml/min was then conducted, while increasing the concentration of acetonitrile up to 30% over 300 minutes. The eluate was monitored by A 220 nm. The fractions containing the desired product were combined together and lyophilized to obtain 66.3 mg of Leu-Phe-Glu-Lys-Ala-Val-Lys-Asp-Tyr-Ile(SEQ ID NO:4).

The paragraph beginning on page 54, line 12 has been amended as follows:

The peptide obtained, Leu-Phe-Glu-Lys-Ala-Val-Lys-Asp-Tyr-Ile(SEQ ID NO:4), had a retention time of 23.8 minutes in an analysis using a reverse phase packing material YMC-PACK ODS-AM column (4.6 ϕ x 250 mm) eluted with a linear gradient of acetonitrile concentration from 12 to 42% containing 0.1% TFA, and the results of amino acid analysis and mass spectrometry of the product were consistent with the theoretical values.

The paragraph beginning on page 55, line 10 has been amended as follows:

(3) Synthesis of SART-3 "284-292" Asn-Tyr-Asn-Lys-Ala-Leu-Gln-Gln-Leu (SEQ ID NO: 5)

According to a similar manner to that described in above (1), using 100 mg of Fmoc-Leu-Alko Resin, Fmoc-Gln-OH, Fmoc-Gln-OH, Fmoc-Leu-OH, Fmoc-Ala-OH, Fmoc-Lys(Boc)-OH, Fmoc-Asn-OH, Fmoc-Tyr(tBu)-OH, and Fmoc-Asn-OH were coupled in order, and the product was then deprotected. The crude peptide obtained was dissolved in aqueous acetic acid and injected into a reverse phase packing material YMC-PACK ODS-A column (30 ϕ x 250 mm) that has been pre-equilibrated with 0.1% aqueous TFA. The column was washed with 0.1% aqueous TFA, and the elution at a flow rate of 7 ml/min was then conducted, while increasing the concentration of acetonitrile up to 30% over 300 minutes. The eluate was monitored by A 220 nm. The fractions containing the desired product were combined together and lyophilized to obtain 25.0 mg of Asn-Tyr-Asn-Lys-Ala-Leu-Gln-Gln-Leu(SEQ ID NO:5).

The paragraph beginning on page 55, line 26 has been amended as follows:

The peptide obtained, Asn-Tyr-Asn-Lys-Ala-Leu-Gln-Gln-Leu(SEQ ID NO:5), had a retention time of 19.0 minutes in an

analysis using a reverse phase packing material YMC-PACK ODS-AM column (4.6 ϕ x 250 mm) eluted with a linear gradient of acetonitrile concentration from 12 to 42% containing 0.1% TFA, and the results of amino acid analysis and mass spectrometry of the product were consistent with the theoretical values.

The paragraph beginning on page 56, line 21 has been amended as follows:

(4) Synthesis of SART-3 "315-323" Ala-Tyr-Ile-Asp-Phe-Glu-Met-Lys-Ile (SEQ ID NO: 6)

According to a similar manner to that described in above (1), using 100 mg of Fmoc-Ile-Alko Resin (0.62mmol/g, 100-200mesh), Fmoc-Lys(Boc)-OH, Fmoc-Met-OH, Fmoc-Glu(OtBu)-OH, Fmoc-Phe-OH, Fmoc-Asp(OtBu)-OH, Fmoc-Ile-OH, Fmoc-Tyr(tBu)-OH, and Fmoc-Ala-OH were coupled in order, and the product was then deprotected. The crude peptide obtained was dissolved in aqueous acetic acid and injected into a reverse phase packing material YMC-PACK ODS-A column (30 ϕ x 250 mm) that has been pre-equilibrated with 0.1% aqueous TFA. The column was washed with 0.1% aqueous TFA, and the elution at a flow rate of 7 ml/min was then conducted, while increasing the concentration of acetonitrile up to 40% over 180 minutes. The eluate was monitored by A 220 nm. The fractions containing the desired

product were combined together and lyophilized to obtain 15.4 mg of Ala-Tyr-Ile-Asp-Phe-Glu-Met-Lys-Ile(SEQ ID NO:6).

The paragraph beginning on page 57, line 11 has been amended as follows:

The peptide obtained, Ala-Tyr-Ile-Asp-Phe-Glu-Met-Lys-Ile(SEQ ID NO:6), had a retention time of 19.6 minutes in an analysis using a reverse phase packing material YMC-PACK ODS-AM column (4.6 ϕ x 250 mm) eluted with a linear gradient of acetonitrile concentration from 21 to 51% containing 0.1% TFA, and the results of amino acid analysis (Met being not detected) and mass spectrometry of the product were consistent with the theoretical values.

The paragraph beginning on page 58, line 7 has been amended as follows:

(5) Synthesis of SART-3 "416-425" Asp-Tyr-Val-Glu-Ile-Trp-Gln-Ala-Tyr-Leu (SEQ ID NO: 7)

According to a similar manner to that described in above (1), using 100 mg of Fmoc-Leu-Alko Resin, Fmoc-Tyr(tBu)-OH, Fmoc-Ala-OH, Fmoc-Gln-OH, Fmoc-Trp(Boc)-OH, Fmoc-Ile-OH, Fmoc-Glu(OtBu)-OH, Fmoc-Val-OH, Fmoc-Tyr(tBu)-OH, and Fmoc-Asp(OtBu)-OH were coupled in order, and the product was then deprotected. The crude peptide obtained was dissolved in

aqueous acetic acid and injected into a reverse phase packing material YMC-PACK ODS-A column (30 ϕ x 250 mm) that has been pre-equilibrated with 0.1% aqueous TFA. The column was washed with 0.1% aqueous TFA, and the elution at a flow rate of 7 ml/min was then conducted, while increasing the concentration of acetonitrile up to 35% over 180 minutes. The eluate was monitored by A 220 nm. The fractions containing the desired product were combined together and lyophilized to obtain 18.9 mg of Asp-Tyr-Val-Glu-Ile-Trp-Gln-Ala-Tyr-Leu(SEQ ID NO:7).

The paragraph beginning on page 58, line 23 has been amended as follows:

The peptide obtained, Asp-Tyr-Val-Glu-Ile-Trp-Gln-Ala-Tyr-Leu(SEQ ID NO:7), had a retention time of 20.5 minutes in an analysis using a reverse phase packing material YMC-PACK ODS-AM column (4.6 ϕ x 250 mm) eluted with a linear gradient of acetonitrile concentration from 25 to 55% containing 0.1% TFA, and the results of amino acid analysis (Trp being not detected) and mass spectrometry of the product were consistent with the theoretical values.

The paragraph beginning on page 59, line 19 has been amended as follows:

(6) Synthesis of SART-3 "426-434" Asp-Tyr-Leu-Arg-Arg-Arg-Val-Asp-Phe (SEQ ID NO: 8)

According to a similar manner to that described in above (1), using 100 mg of Fmoc-Phe-Alko Resin (0.72mmol/g, 100-200mesh), Fmoc-Asp(OtBu)-OH, Fmoc-Val-OH, Fmoc-Arg(Pmc)-OH, Fmoc-Arg(Pmc)-OH, Fmoc-Arg(Pmc)-OH, Fmoc-Leu-OH, Fmoc-Tyr(tBu)-OH, and Fmoc-Asp(OtBu)-OH were coupled in order, and the product was then deprotected. The crude peptide obtained was dissolved in aqueous acetic acid and injected into a reverse phase packing material YMC-PACK ODS-A column (30 ϕ x 250 mm) that has been pre-equilibrated with 0.1% aqueous TFA. The column was washed with 0.1% aqueous TFA, and the elution at a flow rate of 7 ml/min was then conducted, while increasing the concentration of acetonitrile up to 25% over 240 minutes. The eluate was monitored by A 220 nm. The fractions containing the desired product were combined together and lyophilized to obtain 34.0 mg of Asp-Tyr-Leu-Arg-Arg-Arg-Val-Asp-Phe(SEQ ID NO:8).

The paragraph beginning on page 60, line 10 has been amended as follows:

The peptide obtained, Asp-Tyr-Leu-Arg-Arg-Arg-Val-Asp-Phe(SEQ ID NO:8), had a retention time of 20.1 minutes in an analysis using a reverse phase packing material YMC-PACK ODS-

AM column (4.6 ϕ x 250 mm) eluted with a linear gradient of acetonitrile concentration from 12 to 42% containing 0.1% TFA, and the results of amino acid analysis and mass spectrometry of the product were consistent with the theoretical values.

The paragraph beginning on page 61, line 5 has been amended as follows:

(7) Synthesis of SART-3 "448-456" Ala-Phe-Thr-Arg-Ala-Leu-Glu-Tyr-Leu (SEQ ID NO: 9)

According to a similar manner to that described in above (1), using 100 mg of Fmoc-Leu-Alko Resin, Fmoc-Tyr(tBu)-OH, Fmoc-Glu(OtBu)-OH, Fmoc-Leu-OH, Fmoc-Ala-OH, Fmoc-Arg(Pmc)-OH, Fmoc-Thr(tBu)-OH, Fmoc-Phe-OH, and Fmoc-Ala-OH were coupled in order, and the product was then deprotected. The crude peptide obtained was dissolved in aqueous acetic acid and injected into a reverse phase packing material YMC-PACK ODS-A column (30 ϕ x 250 mm) that has been pre-equilibrated with 0.1% aqueous TFA. The column was washed with 0.1% aqueous TFA, and the elution at a flow rate of 7 ml/min was then conducted, while increasing the concentration of acetonitrile up to 30% over 240 minutes. The eluate was monitored by A 220 nm. The fractions containing the desired product were combined together and lyophilized to obtain 22.8 mg of Ala-Phe-Thr-Arg-Ala-Leu-Glu-Tyr-Leu(SEQ ID NO:9).

The paragraph beginning on page 61, line 21 has been amended as follows:

The peptide obtained, Ala-Phe-Thr-Arg-Ala-Leu-Glu-Tyr-Leu(SEQ ID NO:9), had a retention time of 18.1 minutes in an analysis using a reverse phase packing material YMC-PACK ODS-AM column (4.6 ϕ x 250 mm) eluted with a linear gradient of acetonitrile concentration from 20 to 50% containing 0.1% TFA, and the results of amino acid analysis and mass spectrometry of the product were consistent with the theoretical values.

The paragraph beginning on page 66, lines 4-12 has been amended as follows:

Identification of HLA-A2-Restricted Tumor Antigen Peptides

On the basis of the amino acid sequence of tumor antigen protein SART-3 shown in SEQ ID NO: 24, peptide sequences consisting of nine or ten amino acid residues that were expected to be capable of binding to HLA-A0201 were searched on internet using a software of NIH BIMAS (~~http://bimas.dcert.nih.gov/molbio/hla_bind/~~). Those examples of the searched peptides are shown in SEQ ID NOs: 25-52. These peptides were synthesized at Biologica Co. by the Fmoc method.